1/32

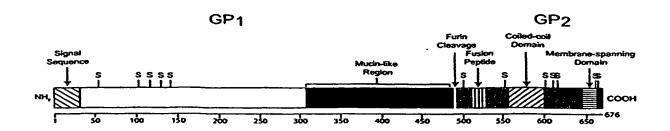


fig. 1A

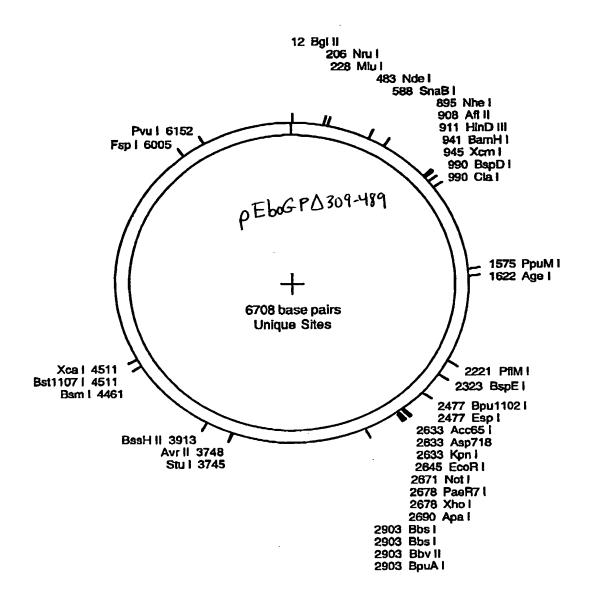


fig. 1B

Positions of Restriction Endonucleases sites (unique sites underlined)

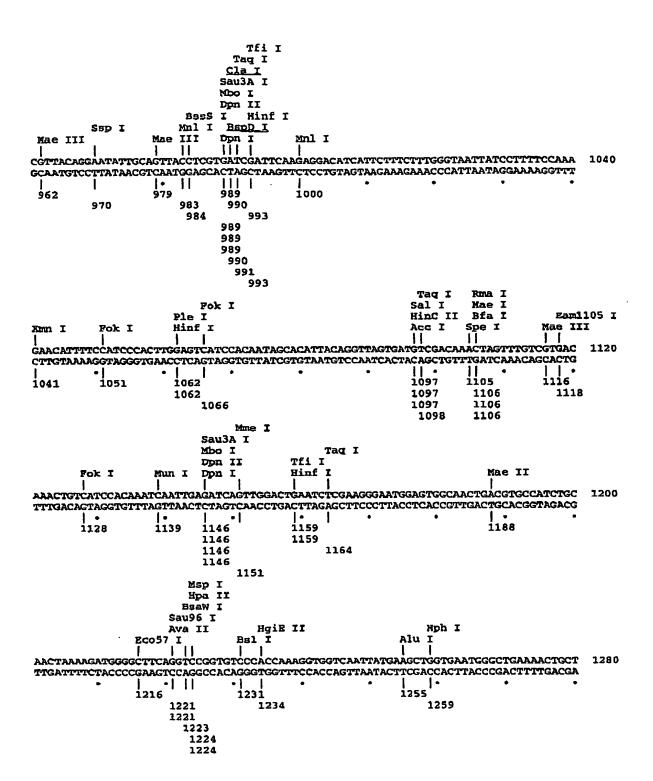
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Sau3A I
            Mbo I
                                   Ple I
    Sau3A I
                    Sau3A I
                                   Hinf I
   Mbo I
            Dpn II
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                                 Taq I
    Dpn II Dpn I
                    Dpn II
                                Sal I
                                                              Aci I
                                                                            Alwn T
   Don I Baty I
                    Dpn I
                                HinC II
                                           Rsa I
                                                             Fnu4H I
                                                                           Bsr I
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          Bal II
                    Alw I
                                Acc I Dde I
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                                                                      Mse I
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GACGGATCGGGAĞATCTCCCGATCCCCTATGGTCGACTCTCAGTACAATCTGCTCTGATGCCGCATAGATAAGCCAGTAT
CTGCCTAGCCCTCTAGAGGGCTAGGGGATACCAGCTGAGAGTCATGTTAGACGAGACTACGGCGTATCAATTCGGTCATA
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            13
                                   35
            13
                                        Cac8 I
                                       Batt I
                                      Hinp I
                                                       Alu I
        Tth111 II
                     Mml I Dde I
                                      Hha I
                                                   Mse I
                                      111
CTGCTCCCTGCTTGTGTGTTGGAGGTCGCTGAGTAGTGCGCGAGCAAAATTTAAGCTACAACAAGGCAAGGCTTGACCGA 160
GACGAGGGACGAACACACACCTCCAGCGACTCATCACGCGCCTCGTTTTAAATTCGATGTTCCCTTCCCGAACTGGCT
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                                        Bbv I
                                                                      BstU I
                                      HinP I
                                               BstU I
                                                          Sau96 I
     Nla III
                                                                     Mlu I
Mun I
         Mbo II
                   Dde I
                                      Hha I
                                              Nru I Rsa I
                                                                     Afl III
CAATTGCATGAAGAATCTGCTTAGGGGTTAGGGGTTTTGCGCTGCTTCGCGATGTACGGGCCAGATATACGCGTTGACATT
GTTAACGTACTTCTTAGACGAATCCCAATCCGCAAAACGCGAAGGGGTACATGCCCGGTCTATATGCGCAACTGTAA
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                                                                      229
            173
                                        200
                                                                         232
         Rma I
         Mae I
                                                                         Mae III
         Bfa I Mse I
                                                                      BstU I
        Spe I Ase I
                                                      Bşl I
                                                                     Aci I
GATTATTGÁCTAGTTÁTTAATAGTAATCAATTACGGGGTCATTAGTTCATAGCCCATATATGGAGTTCCGCGTTACATAA
CTAATAACTGATCAATAATTATCATTAGTTAATGCCCCAGTAATCAAGTATCGGGTATATACCTCAAGGCGCAATGTATT
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ScrF I
                 ECOR II
                 BstN I
              Aci I
                                                 Mae II
            Cac8 I
            Bgl I
                                                BsaH I
                                                Aha II
           Sau96 I
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                          Aci I
                                       Aci I
                                                Aat II
                                                             Mae II
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           333
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                 339
                       Mae II
                      BsaH I
                      Aha II
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                                                                 Rsa I
                      Aat II
AACGCCAATAGGGACTTTCCATTGACGTCAATGGGTGGACTATTTAGGGTAAACTGCCCACTTGGCAGTACATCAAGTGT
TTGCGGTTATCCCTGAAAGGTAACTGCAGTTACCCACCTGATAAATGCCATTTGACGGGTGAACCGTCATGTAGTTCACA
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                         BsaH I
                         Aha II
Aat II
                                                                 Rsa I
                                            Sau96 I
                                                              Bsr I
                                            Hae III
  Nde_I
            Rsa I
ATCATATCCCAAGTACGCCCCCTATTGACGTCAATGACGGTAAATGGCCCGCCTGGCATTATGCCCAGTACATGACCTTA
TAGTATACGGTTCATGCGGGGGGATAACTGCAGTTACTGCCATTACCGGGCGGACCGTAATACGGGTCATGTACTGGAAT
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                                                 Nla III
                                                Sty I
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                                                NCO I
                                                Dsa I Sfan I
                          SnaB I
                                                BaaJ I
                                                                      Rsa I
                    Rsa I BsaA I
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TGGGACTTTCCTACTTGGCAGTACATCTACGTATTAGTCATCGCTATTACCATGGTGATGCGGTTTTGGCAGTACATCAA
ACCCTGAAAGGATGAACCGTCATGTAGATGCATAATCAGTAGCGATAATGGTACCACTACGCCAAAACCGTCATGTAGTT
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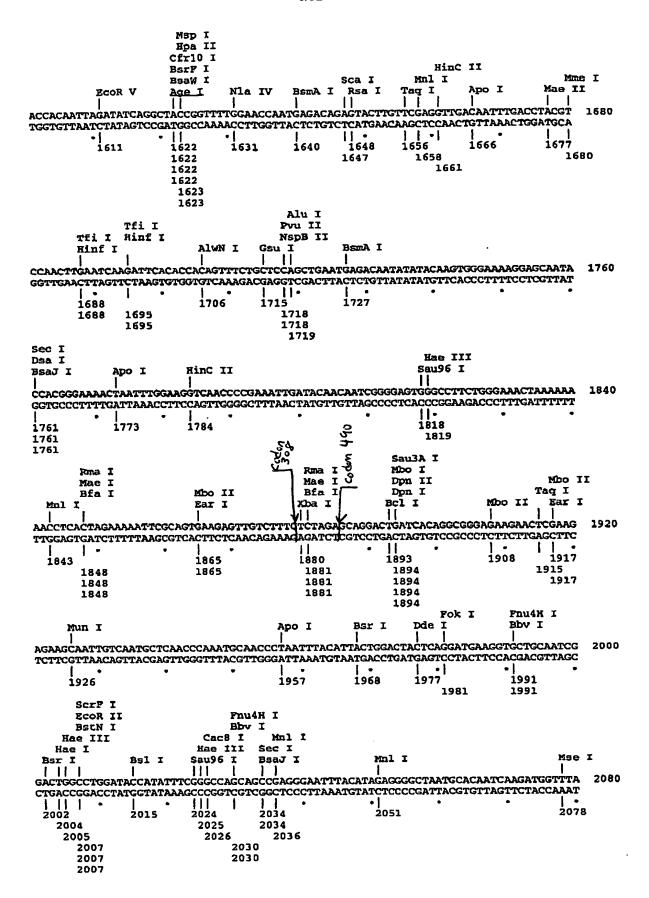
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942

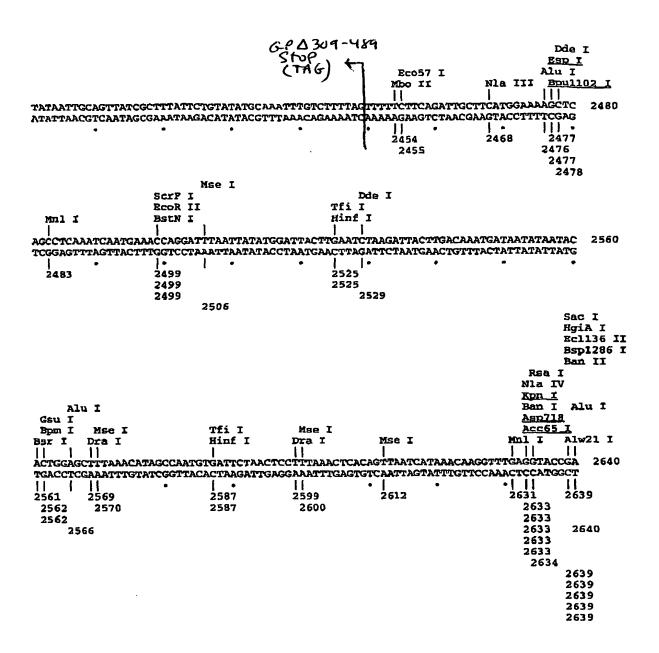
5/32



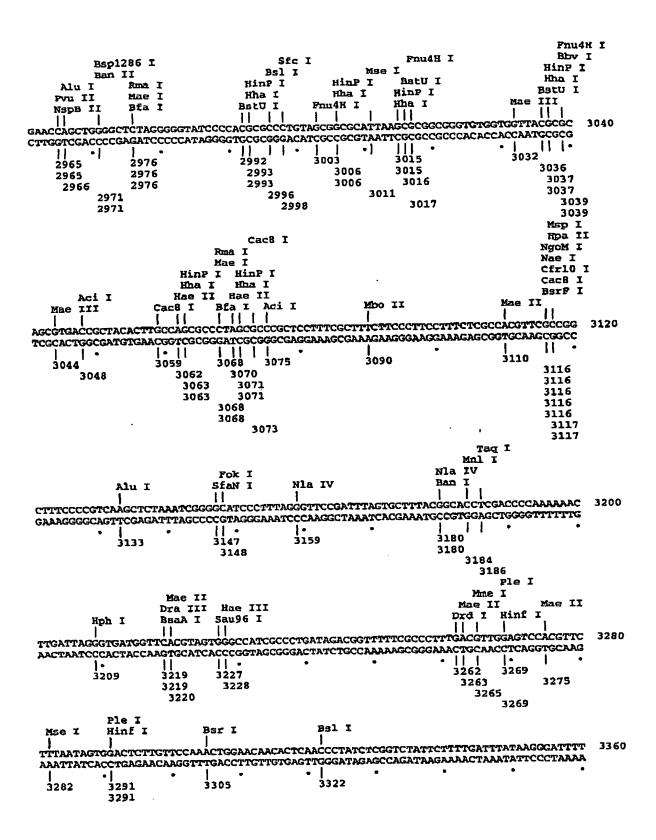
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Cfr10 I
                                                                             Nla IV
                                                                             Ban I
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                                                                          ScrP I
                                                                          Nci I
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                                                                          Bal I
                                                Hha I
                                                                          Bon I Msp I
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BsaJ I Hpa II
                                                            Tfi I
                                             Fnu4H I
                                                            Hinf I
                                     Acc 1
                                             Bbv I
ACAATCTTGAAATCAAAAAACCTGACGGGAGTGACTGTCTACCAGCAGCGCCAGACGGGATTCGGGGCTTCCCCCGGTGC
TGTTAGAACTTTAGTTTTTTGGACTGCCCTCACTCACAGATGGTCGTCGCGGTCTGCCCTAAGCCCCGAAGGGGGCCCACG
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                               Bel I
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      Bsp1286 I
                            Ava II
                                      Map I
      ApaL I
                                                       Bal I Mnl I
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      Alw21 I
                           Nla IV
                                      Hpa II
CGGTATGTGCACAAAGTATCAGGAACGGGACCGTGTGCCGGAGACTTTGCCTTCCATAAAGAGGGTGCTTTCCTGTA 1440
GCCATACACGTGTTTCATAGTCCTTGCCCTGGCACACGCCTCTGAAACGGAAGGTATTTCTCCCACGAAAGAAGGACAT
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                               1391
      1367
   Tag I
 Sau3A I
                              Mol I
 Mbo I
                            Sec I
 Don II
                                                                                  Alu I
                            BsaJ I
                                              Eco57 I
 Dpn I
TGATCGACTTGCTTCCACAGTTATCTACCGAGGAACGACTTTCGCTGAAGGTGTCGTTGCATTTCTGATACTGCCCCAAG
                                                                                     1520
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                                              1485
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              Eco57 I
     Xmm I
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 Dde I
 CTAAGAAGGACTICTTCAGCTCACACCCCTTGAGAGAGCCGGTCAATGCAACGGAGGACCCGTCTAGTGGCTACTATTCT 1600
 GATTCTTCCTGAAGAAGTCGAGTGTGGGGAACTCTCTCGGCCAGTTACGTTGCCTCCTGGGCAGATCACCGATGATAAGA
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Hae III
                  Msc I
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                Cac8 I
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                                    Alu I
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ATCTGTGGGTTGAGACÁĞCTĞGCCAACĞAGACĞACTCAAGCTCTTCAACTGTTCCTGAGAGCCACAACTGAGCTACGCAC 2160
TAGACACCCAACTCTGTCGACCGGTTGCTCTGCTGACTTCGAGAACTTGACAAGGACTCTCGGTGTTGACTCGATGCGTG
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        Hml I
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CTTTTCAATCCTCAACCGTAAGCCAATTGATTTCTTGCTGCAGCGATGGGGCCGCACATGCCACATTCTGGGACCGGACT 2240
GAAAAGTTAGGAGTTGGCATTCCGTTAACTAAAGAACGACGTCGCTACCCCGCCGTGTACGGTGTAAGACCCTGGCCTGA
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GCTGTAŤCGAAĊCAĊATGATTĠGACCAAGACATAACAGACAAAATŤĠATCAGATTATŤĊATGATTTGTTGATAAAACC 2320
CGACATAGCTTGGTGTACTAACCTGGTTCTTGTATTGTCTGTTTTTAACTAGTCTAATAAGTACTAAAAACAACTATTTTGG
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   Msp I
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                                                     Hpa II
   Bsl I
                                                    Cfr10 I
  BSDE I
                                        BsmA I
                                   Fok I
                                                    Barf I
                                                                    Mae III
  BsaW I
                       Mun I
GAAGGCCTGGTCCCCCTGTTACTGTTAACCACCTGTCCTACCTCTGTTACCTATGGCCGTCCATAACCTCAATGTCCGCA
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Sau96 I
                                Xho I
                                           Sau96 I
                                PacR7 I
                                           Nla IV
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                             Fnu4H I
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                                                            Sau3A I
                                       Rma I
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T Bfa I Pme I NspB II
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GCTCGAATTCTGCAGATATCCAGCACAGTGGCGGCCGCTCGAGTCTAGAGGGCCCGTTTAAACCCGCTGATCAGCCTCGA 2720
CGAGCTTAAGACGTCTATAGGTCGTCACCGCCGCGAGCTCAGATCTCCCGGGCAAATTTGGGCGACTAGTCGGAGCT
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GTCCTTTCCTAATAAAATGAGGAAATTGCATCGCATTGTCTGAGTAGGTGTCATTCTATTCTGGGGGGTGGGGTGGGGCA 2880
2828
                                   2840
                2819
                                 Nla III
                                Sph I
                                NapH I
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                    Boua I
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                                Cac8 I
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                                         Fok I
                                                 Ban II
                                                             Dde I
                             Cac8 I
            Mnl I
                    Bbs I
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GGACAGCAAGGGGAGGATTGGGAAGACAATAGCAGGCATGCTGGGGATGGGGTGGGCTCTATGGCTTCTGAGGCGGAAA 2960
CCTGTCGTTCCCCCTCCTAACCCTTCTGTTATCGTCCGTACGACCCCTACGCCACCCGAGATACCGAAGACTCCGCCTTT
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Apo I
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CCCCTARAGCCGGATRACCAATTITTTACTCGACTAAATTGTTTTTAAATTGCGCTTAATTAAGACACCTTACACACAGT
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                                 Nla III
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        SCYF I
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                               Mpo I
       Bon I
                               Don II
      Xma I
                               Dpn I
      Sma I
                               Bcl I
      Sec I
      ScrF I
                           Sau3A I
                                        Hin¢ II
                           Mbo I
                                     Mae II
      Nci I
                                     Afl III
                           Don II
      BsaJ I
                                    Pml I
      Bcn I
                           Don I
                           BstY I
                                    Eco72 I
                                               Mse I
      AVA I
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                                    Bsaa I
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WO 03/102219

BsaH I Aha II BstU I Hae III BstV I Mac I HinP I Hae I Hha I Eae I Cac8 I Nla III HgiA I Bsp1286 I HimP I Sty I Alw21 I BESH II Sec I BstU I Mae II Msp I Nco I Aci I Aat II Dsa I Bar I Hpa II Mnl I Bsa.7 I HinC II Bsaw I Hph I Hha I Hph I]] 3900 | •|||||| || 3908 3915 || ||• 3875 3885 3861 3890 3901 3911 3919 3864 3875 3912 3920 3901 3875 3904 3913 3875 3915 3904 3875 3913 3904 3876 3913 3878 3878 3913 3914 3878 3916 3879 3919 3919 ScrP I Nci I MSD I Hpa II Bcn I Msp I Xma I Hpa II Sma I Rgie II Sec I Cfr10 I ScrF I Map I Sau96 I BSTF I BsiE I Nci I Hpa II BeaJ I BarB I BsiE I Cfr10 I Sau96 I Bcn I Msp I BSTF I Ava II Mnl I Taq I Ava II Ava I Ava I Hpa II TOGCCGGAGCGCTCGAGTTCTGGACCGGCTCGGGTTCTCCCGGGACTTCGTGGAGGACGACTTCGCCGGTGTGG 4000 CAGCGGCCTCGCCAGCTCAAGACCTGGCTGGCCGAGCCCAAGAGGGCCCCTGAAGCACCTCCTGCTGAAGCGGCCACACC | 3955 || 3965 | |• | | 3926 39 | 3944 1 11 •11 3999 3979 3991 3935 3991 3926 3944 3965 3948 3965 3992 3929 3992 3999 3950 3965 3932 3965 3950 3950 3965 3951 3965 3951 3965 3966 3966

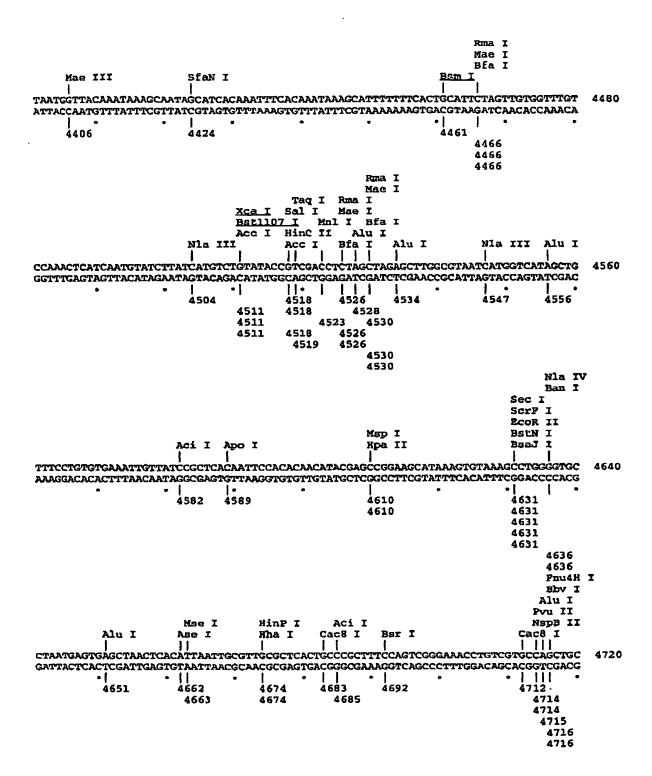
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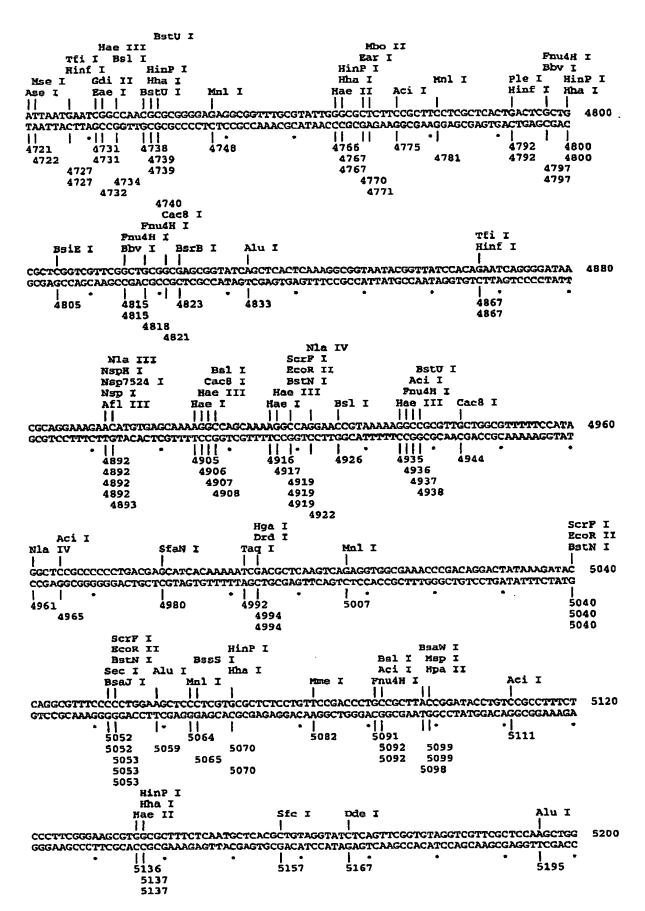
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Sec I
                                                           ScrF I
                                                           ECOR II
                                                           BstN I
                                                           Bal I
                                                           BsaJ I
                                    ScrF I
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                              ScrF I
                                                        Hae I
                              ECOR II
                                                      ScrP I
                              BatN I
                                                      EcoR II
                           Sau96 I EcoR II
Ava II BStN I
ScrF I
                                                      BatN I
Nci I
                                            Msp I
                                                      Bsl I
Map I
                         Batu I Sau96 I
                                             Hpa II
                                                      Sec I
Rpa II
         Mae III
                        HinP I
                                II sva
                                         Nla IV
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AGGCCCTGCTGCACTGGGACAAGTAGTCGCGCCAGGTCCTGGTCCACCACGGCCTGTTCTCGGGACCGGACCCCACACCCAC
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MSD I
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             Sec I
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                                       Bcn I
  Sau3A I
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                                 Batu I Hae III
Hinp I Baik I
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            Bgl I
  Mbo I
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                                                     Alw21 I
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          Pnu4H I
                                                              Eae I
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             4176
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                                       4206
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                                                                   SCTF I
          Mae II
                                                                   Nci I
          Pml I
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                          Tfi I
                                  Aci I
          Eco72 I
                                                                   Hpa II
                         Hinf I Pnu4H I
                                                          rfi I
          BsaA I
                                                          Rinf I
                                                                   Bcn I
         Afl III
                        I per
                              Aci I
AGCAGGACTGACACGTGCTACGAGATTTCGATTCCACCGCCGCCTTCTATGAAAGGTTGGGCTTCGGAATCGTTTTCCGG
TCGTCCTGACTGTGCACGATGCTCTAAAGCTAAGGTGGCGGCGGAAGATACTTTCCAACCCGAAGCCTTAGCAAAAGGCC
                        | |
4268
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          4252
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           4253
    MSD I
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                  Bsl I
                           Sau3A I
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                           Mbo I
                Gsu I
   Nae I
             sau3A I
                           Don II
   Cfrl0 I
                          BstY I
             Mbo I
   Cac8 I
                          Alw I
   BarP I
             Don II
                                                                  Alu I
                     HinP I
                                   Gsu I
             Dpn I
 Hga I
                                                                Pnu4H I
                    Hha I Don I
                                   Bom I
 BSAH I
 Alw I
 CTGCGGCCGACCTACTAGGAGGTCGCGCCCCTAGAGTACGACCTCAAGAAGCGGGTGGGGTTGAACAAATAACGTCGAAT
                                                                 4393
                          || |
| 4356
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31 4338 4345
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4331
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                     4344
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    4324
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    4324
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     4325
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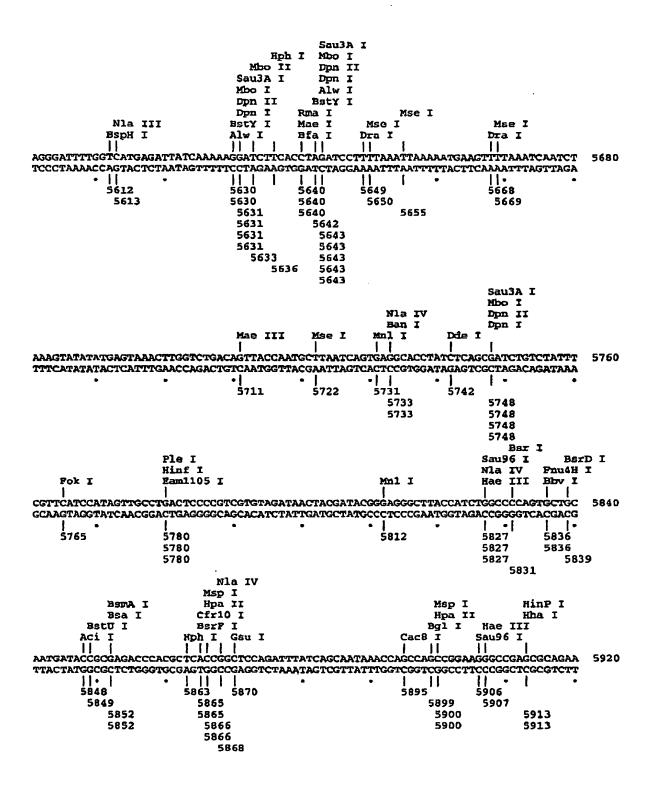
10/8 8570

18/32





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HinP I
                                                                      Msp I
                                Fnu4H I
                                                                     Hpa II
                                                                    ScrP I
    HgiA I
                                Bbv I
                                              Mae III
                                            MSD I
    Bsp1286 I
                              NspB II
                                                               Mme I
    Apal I
                              Aci I
                                            Hpa II
                                                             Ple I Nci I
    Alw21 I
                                                             Hinf I Bon I
                           BsiE I Hha I
                                           BsaW I
                                           11
                                              1
                              1 1
GCTGTGTGCACGAACCCCCGTTCACCCGGACCGCTGCGCCTTATCCGGTAACTATCGTCTTGAGTCCAACCCGGTAAGA
CGACACACGTGCTTGGGGGGCAAGTCGGGCTGGCGACGCGGAATAGGCCATTGATAGCAGAACTCAGGTTGGGCCATTCT
                                           5245
                           [• [ ] ·
                                   5237
                                                             5263
                                                                     5271
                            5229
     5206
    5206
                              5232
                                            5246
                                                             5263
                                                                     5271
                                            5246
                                                                5266
    5206
                              5232
    5206
                                5234
                                               5249
                                                                     5271
                                                                      5272
                                5234
                                                                      5272
                                   5237
                     Alwn I
                    Fnu4H I
                 Pnu4H I
                 Bbv I
                          Bsr I
             Bsr I Bbv I
                                                 Mnl I
                                                                  SEc I
                              Mae III
                    H
CACGACTTATCGCCÁCTGGCAGCAGCCÁCTGGTAACAGGATTAGCAGAGCGAGGTATGTAGGCGGTGCTACAGAGTTCTT 5360
GTGCTGAATAGCGGTGACCGTCGCTGACCATTGTCCTAATCGTCTCGCTCCATACACCCCCCACGATGTCTCAAGAA
                 | • | |
5 5302
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                                                 5331
                                                                  5348
              5295
                              5312
                 5299
                          5308
                  5299
                    5302
                      5303
         Bsl I
                         Roma I
       Hae III
                         Mae I
                                                 HinP I
                         Bfa I
                                                 Hha I
                                                         Eco57 I Mae III
       Hae I
GAAGTGGTGGCCTAACTACGGCTACACTAGAAGGACAGTATTTGGTATCTGCGCTCTGCTGAAGCCAGTTACCTTCGGAA 5440
CTTCACCACCGGATTGATGCCGATGTGATCTTCCTGTCATAAACCATAGACGCGAGACGACTTCGGTCAAATGGAAGCCTT
                                                •|
5411
       ||•|
5368
                         5387
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                                                                  5428
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                                                               5425
       5369
                         5387
          5371
                         5387
                    Map I
                    Hpa II
                                                                  Fnu4H I
                  Sau3A I
                                                                  Bbv I
                  Mbo I
                  Dpn II
                                   II Egen
                                                               Tthill II
                                                                              HinP I
                               HgiR II
                                                              Cac8 I
                                                                              Hha I
                  Dpn I
                                                                             BstU I
           Alu I Alw I Tth111 II Aci I
                                                         Tthlll II
<u>ANAGAGTTGGTÄGCTCTTGATCCGGCANACANÀCCACCGCTGGTAGCGGTGGTTTTTTTTTGCANGCAGCAGCAGATTACG</u>
11 1 -
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                  1- |
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                  5459
                                    5477
           5452
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                                    5477
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                                                                  5508
                                                                  5508
                  5459
                     5462
                     5462
                        Sau3A I
             Sau3A I
                        Mbo I
             Mbo I
                        Dpn II
             Dpn II
                        Dpn I
                                Sau3A I
             Don I
                        Alw I
                                Mbo I
                                                      Dde I
            BstY I
                      BstY I
                                Dpn II
                                                                            Mse I
                     Mbo II
                                                                         Mae II
            Alw I
                                                  Нда I
                                Dpn I
CGCAGAAAAAAGGATCTCAAGAAGATCCTTTGATCTTTTCTACGGGGTCTGACGCTCAGTGGAACGAAAACTCACGTTA
GCGTCTTTTTTCCTAGAGTTCTTCTAGGAAACTAGAAAAGATGCCCCAGACTGCGAGTCACCTTGCTTTTGAGTGCAAT
                  • | ||
5542
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Alu I
                                      ScrP I
                                      Nci I
                                      Msp I
                                             Rma I
                Mnl I Bsr I Mse I
                                      Hpa II Mae I
                                                               Mse I
              Aci I Fok I
 Ava II
                            Ase I
                                             Bfa I
                                      Bon I
                                                            Bsr I
                             11
GTÉGTCCTGCAACTTTATCCGCCTCCATCCAGTCTÁTTAATTGTTGCCGGGAÁGCTAGAGTAAGTAGTTCGCCAGTTAAT 6000
|• | | |•
5939 5946
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                                             5975
                                       5967
                                       5967
                                       5967
                                            5973
                                                                 Nla IV
        Mae II
                                                                Msp I
    HinP I
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                                                             Sau3A I
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                     Dpn II
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      Sau3A I
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      Mbo I
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                     Alw I
      Dpn II
                   Nla III
                                                      Sau96 I
      Dpn I
               Mae III
                           Nla III
                                              Alu I
                                                      Ava II Dpn I
                                                      1 1
TTCCCAACGATCAAGGCGAGTTACATGATCCCCCATGTTGTGCAAAAAAGCGGTTAGCTCCTTCGGTCCTCCGATCGTTG
AMGGTTGCTAGTTCCGCTCAATGTACTAGGGGGTACAACACGTTTTTTCGCCAATCGAGGAAGCCAGGAGGCTAGCAAC
                                                      6145
      6089
                6100
                            6114
                                              6136
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                   6104
      6089
                                                      6145
      6089
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                                                        6148
      6089
                                                            6152
                      6107
                      6107
                                                            6152
                      6107
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                      6107
                                                             6153
                                                             6153
            Aci I
           Pnu4H I
          Hae III
          Gđi II
                                  Fnu4H I
                                                             Fok I
                          Nla III
                                  Bbv I
                                                        Nla III
          Rae T
                                            Apo I
          1111
TCAGAAGTAAGTTGGCCGCAGTGTTATCACTCATGGTTATGGCAGCACTGCATAATTCTCTTACTGTCATGCCATCCGTA 6240
||||
6173
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6202
                          6192
                                            6213
                                                         6228
          6173
                                  6202
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           6174
           6175
            6176
                                                                  Msp I
                                                                  Hpa II
              Hph I
                                                                 ScrF I
          Bsr I Rsa I
Mae III Sca I
                                                   BsiR I
                                                                 Nci I
 SfaN I
                                               Pnu4H I
                                  Dde I
                                                                 Ben I
AGATGCTTTTCTGTGACTGGTGAGTACTCAACCAAGTCATTCTGAGAATAGTGTATGCGGCGACCGAGTTGCTCTTGCCC
TCTACGAAAAGACACTGACCACTCATGAGTTGGTTCAGTAAGACTCTTATCACATACGCCGCTGGCTCAACGAGAACGGG
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Acc I

Acc65 I

Bsp1286 I

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Psp I

11

PCT/US03/17577

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Hinp I
                                            HqiA I
                                            Bsp1286 I
                    Hha I
                                                            Mae II
ReaH I
                    BstV I
                                      Mse I
                                                         Xmm I Mbo II
                                     Dra I Alw21 I
Aha II
                   Aci I
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                   111
GGCGTCAATACGGGATAATACCGCGCCACATAGCAGAACTTTAAAAGTGCTCATCATTGGAAAACGTTCTTCGGGGCGAA 6400
CCGCAGTTATGCCCTATTATGCCGCGGTGTATCGTCTTGAAATTTTCACGAGTAGTAACCTTTTGCAAGAAGCCCCGCTT
                                                            ) ) .
6321
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6341
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6360
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                                                         6380
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                                            6367
6322
                     6343
                     6343
                                            6367
                            Bar I
                          Sau3A I
                                                                Eco57 I
         Sau3A I
                                                              Moo II
         Mbo I
                                                 HgiA I
                          Moo I
                                                             Sau3A I
         Dpn II
                          Dpn II
                                                 Bsp1286 I
                                                 ApaL I
                                                             Mbo I
                          Dpn I
         Don I
                                                             Dpn II
        BstY I NSpB II
                         Alw I
                                      Mae III
                                                 Alw21 I
                                              BSSS I
                                                             Don I
         Alw I Aci I
                         BstY I
                                 Taq I
AACTCTCAAGGATCTTACCGCTGTTGAGATCCAGTTCGATGTAACCCACTCGTGCACCCAACTGATCTTCAGCATCTTTT
TTGAGAGTTCCTAGAATGGCGACAACTCTAGGTCAAGCTACATTGGGTGAGCACGTGGGTTGACTAGAAGTCGTAGAAAA
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                                                               6466
                                                  6452
          6411
                          6428
                                                                6467
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                             6431
                                            Aci I
                                            Fru4H I
    Hph I
                  Hph I
ACTITICACCAGCGTTTCTGGGTGAGCAAAAACAGGAAGGCAAAATGCCGCAAAAAAGGGAATAAGGGCAACACGGAAATG
TGARAGTGGTCGCARAGACCCACTCGTTTTTGTCCTTCCGTTTTACGGCGTTTTTTCCCTTATTCCCGCTGTGCCTTTAC
                                            6526
    6485
                   6500
                                             6527
                                                             BarB I
                                                          Nla III
                                                         BapH I
             Mbo II
                         Sap I
                                                       Bank I
             Ear I
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AACTTATGAGTATGAGAAGGAAAAGTTATAATAACTTCGTAAATAGTCCCAATAACAGAGTACTCGCCTATGTATAAAC
                                                       | || |
6617
             6574
                          6587
                                                          6620
              6575
                                                           6621
                                                              6624
                                                                Tag I
                                                                Sal I
                                                               HinC II
                                                               Acc I
                                 HinP I
                                                             Mae II
                                 Hha 1
                                                             Beal I
                                BstU I
                               Aci I
                                                             Aha II
                           Mla IV
                                                             Aat II
                                                             11 11
AATGTATTTAGAAAAATAAACAAATAGGGGTTCCGCGCACATTTCCCCGAAAAGTGCCACCTGACGTC
 TTACATAAATCTTTTTATTTGTTTATCCCCAAGGCGCGTGTAAAGGGGCTTTTCACGGTGGACTGCAG
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                               111
                            6669
                                                             6703
                               6673
                                 6674
                                                             6703
                                                              6704
                                 6675
                                                                6706
                                  6675
                                                                6706
                                                                6706
                                                                 6707
     Restriction Endonucleases site usage
                                                    Nep7524 I
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Aat II
                  Ben I
                                                     NapB II
                                    Fok I
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                  Bema I
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NspH I

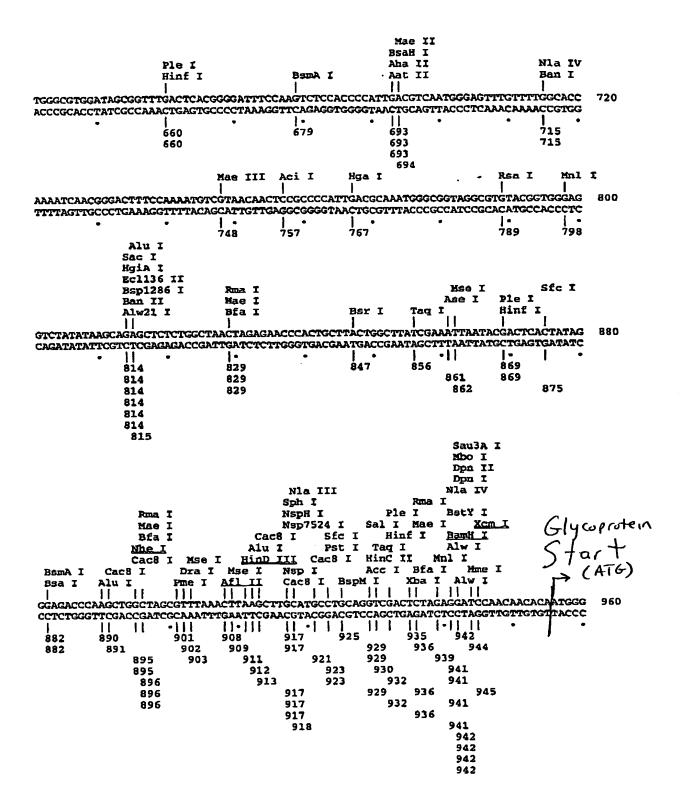


fig. 1C

25/32

WO 03/102219

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TEI I
                              Taq I
                             Cla I
                            Sau3A I
                            Mbo I
                            Dpn II
                       Bses I Hinf I
        Ssp I
                     Mnl I BspD I
Mae III
                  Mae III
                            Dpn I
                                       Mnl I
                            ΠÏΪĪ
CÓTTACAGGÁATATYGCAÓFTACCTCGTGÁTCGATTCAAGAGGACATCATTCTTTCTTTGGGTAATTATCCTTTTCCAAA 1040
<u>GCAATGTCCTTATAACGTCAATGGAGCACTAGCTAAGTTCTCCTGTAGTAAGAAAGCCCATTAATAGGAAAAGGTTT</u>
                  1- 11
                            111 1
 962
                  979
                            989
                                        1000
                      983
                             990
                       984
                                993
                            989
                            989
                            989
                             990
                              991
                                993
                                                          Tag I
                                                                  Runa I
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TTTGACAGTAGGTGTTTAGTTAACTCTAGTCAACCTGACFTAGAGCTTCCCTTACCTCACCGTTGACTGCACGGTAGACG
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TTGATTTTCTACCCCGAAGTCCAGGCCACAGGGTGGTTTCCACCAGTTAATACTTCGACCACTTACCCGACTTTTGACGA
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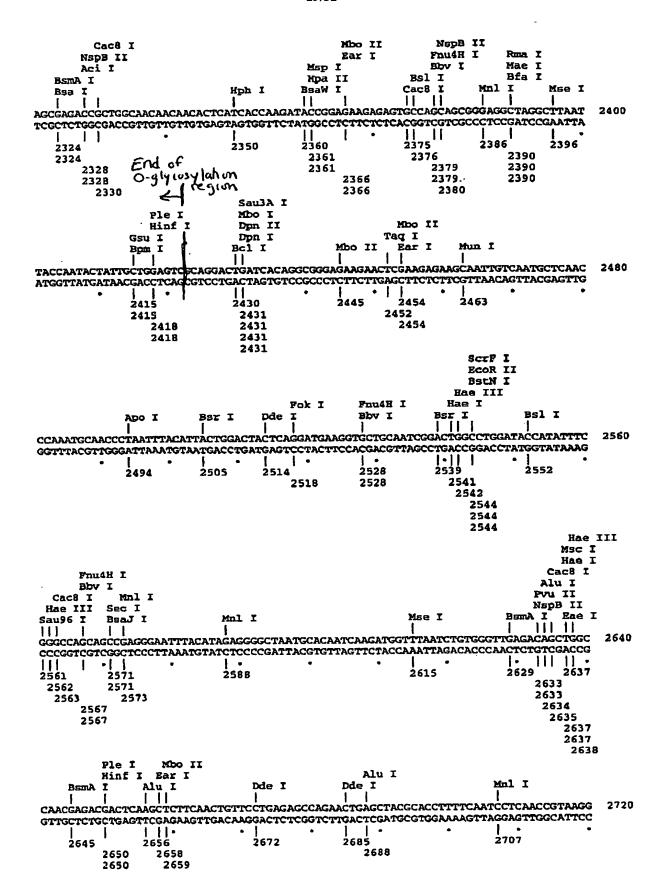
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TGTTAGAACTTTAGTTTTTTTGGACTGCCCTCACTCACAGATGGTCGTCGCGGTCTGCCCCTAAGCCCCGAAGGGGGGCCACG
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                             Bsl I
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GCCATACACGTGTTTCATAGTCCTTGCCCTGGCACACGGCCTCTGAAACGGAAGCTATTTCTCCCACGAAAGAAGGACAT
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   Taq I
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CATTCTTCCTGAAGAAGTCGAGTGTGGGGAACTCTCTCGGCCAGTTACGTTGCCTCCTGGGCAGATCACCGATGATAAGA
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Msp I Hpa II Cfr10 I Hinc II BsrF I Mma I Mnl I BsaW I Sca I Apo I Mae II Nla IV BsmA I Rsa I Tag I ECOR V I_SPA 11 1 1 П accacaattagatatcaggctáccgottttggaaccaatgagacagágtacttgttcgaggttgacaatttgacctacgt 1680 TGGTGTTAATCTATAGTCCGATGGCCAAAACCTTGGTTACTCTGTCTCATGAACAAGCTCCAACTGTTAAACTGGATGCA 11. 1 1 -1 1631 1640 1648 1656 **1666** 1677 1611 1622 1658 1680 1647 1622 1661 -1622 1622 1623 1623 Alu I Pvu II Tfi I Tfi I Hinf I NapB II BSMA I AlwN I Gsu I Hinf I CCAACTTGAATCAAGATTCACACCACAGTTTCTGCTCCAGCTGAATGAGACAATATATACAAGTGGGAAAAGGAGCAATA 1760 GGTTGAACTTAGTTCTAAGTGTGGTGTCAAAGACGAGGTCGACTTACTCTGTTATATATGTTCACCCTTTTTCCTCGTTAT | ||-1715 1727 1706 1688 1718 1695 1688 171B 1695 1719 Sec I Hae III Dsa I HinC II . Sau96 I Apo I **BSAJ I** CCACGGGAAAACTAATTTGGAAGGTCAACCCCGAAATTGATACAACAATCGGGGAGTGGGCCTTCTGGGAAACTAAAAAA 1840 GGTGCCCTTTGATTAAACCTTCCAGTTGGGGCTTTAACTATGTTGTTAGCCCCTCACCCGGAAGACCCTTTGATTTTT 11**i784** 1818 1773 1761 1819 1761 start of O-glycosylation region 1761 Rma I Mae I Ple I Mbo II Bfa I Hinf I Rar I Mnl I AACCTCACTAGAAAAATTCGCAGTGAAGAGTTGTCTTTCACAGTTGTATCAAACGGAGCCAAAAACATCAGTGGTCAGAG 1920 TTGGAGTGATCTTTTTAAGCGTCACTCTCAACAGAAAGTGTCAACATAGTTTGCCTCGGTTTTTGTAGTCACCAGTCTC 1 • 1918 i895 1865 **1843** 1918 1848 1865 1848 1848 Sau96 I Sec I ScrP I ECOR II BatN I Mbo II BsaJ I BstV I BpuA I Bbv II Sec I HinP I Hha I Bsl I Msp I Xmm I Mme I Bbs I Ava II Eco57 I BerD I Bbs I Nla IV Nla III Mnl I Mbo II BsaJ I Eco57 I Hpa II 1 1 TCCGGCGCGAACTTCTTCCGACCCAGGGACCAACACAACAACTGAAGACCACAAAATCATGGCTTCAGAAAATTCCTCTG 2000 AGGCCGCGCTTGAAGAAGGCTGGGTCCCTGGTTGTGTTGTTGACTTCTGGTGTTTTAGTACCGAAGTCTTTTAAGGAGAC | || • || || • 1934 1942 · | | 1962 1 • 1 1 11 1. 1978 1995 1922 2000 1946 1983 1937 1964 1964 1925 1938 1947 1925 1942 1964 1964 1943 1926 1964 1943 1943 1943 1943 1947

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GTTACCAAGTTCACGTGTCAGTTCCTTCCCTTCGACGTCACAGCGTAGATTGTTGGGAACGGTGTTAGAGGTGCTCAGGG
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TCAAGTTGAACAACATCACCGCAGAACAGACAACGACAGCCACGCCTCCGACACTCCCTCTGCCACGACCGCCGGAC
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AGTTCAACTTGTTGTAGTGGCGTCTTGTCTGTTGCTGTCGGTGTCGGAGGCTGTGAGGGAGACGGTGCTGGCGTCGGCCTG
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GGGGTTTTCGTCTTGTGGTTGTGCTCGTTCTCGTGACTGAAGGACCTGGGGCGCTCGTCTTCTTCAGGGGTTTTGGTG
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Pfim I
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                 Pnu4H I
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               Pst I
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              Pnu4H I
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                                                                    Taq I Nla III
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GTTAACTAAAGAACGACGTCGCTACCCCGCCGTGTACGGTGTAAGACCCTGGCCTGACGACATAGCTTGGTGTACTAACC
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                                                                       Sec I
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ACCAAGAACATAACAGACAAAATTGATCAGATTATTCATGATTTTGTTGATAAAACCCTTCCGGACCAGGGGACAATGA
TGGTTCTTGTATTGTCTGTTTTAACTAGTCTAATAAGTACTAAAACAACTATTTTGGGAAGGCCTGGTCCCCCTGTTACT
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                                     BSDM I
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Mun I
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GTTAACCACCTGTCCTACCTCTGTTACCTATGGCCGTCCATAACCTCAATGTCCGCAATATTAACGTCAATAGCGAAATA
                                 2911
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 2881
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               Glycoprokin
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                  STUP
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                                                            Dde I
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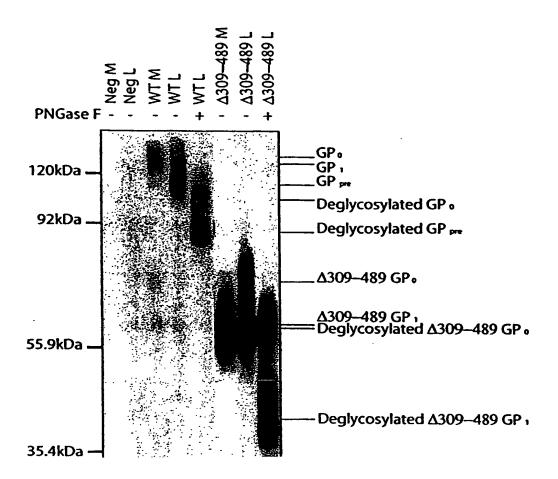
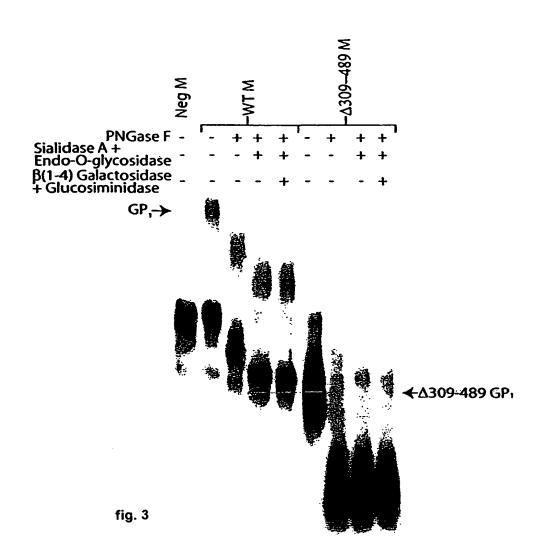


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